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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,003	11/30/2001	Craig A. Rosen	PA003P1	7261

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EXAMINER	
SPIEGLER, ALEXANDER H	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,003	ROSEN ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,28-33 and 36-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,28-33 and 36-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. This action is in response to Applicants' response, filed on February 17, 2004. Currently, claims 25, 28-33 and 36-40 are pending and are herein rejected. This action is made NON-FINAL, as this action contains rejections that were not necessitated by Applicants' amendments. Any objections and rejections not reiterated below are hereby withdrawn.

2. The examiner has changed for this application.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 25, 28-33 and 36-40 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility, or in the alternative, a well established utility.

The specification teaches SEQ ID NO: 22 (which encodes SEQ ID NO: 41) is "GENE NO: 12" (see pages 71 and 108, Tables 1-2 and page 64, line 25). Specifically, the specification teaches the "translation product of this gene shares sequence homology with glutathione peroxidase-related proteins (See e.g., Genbank Accession Nos. emb/CAB43534.1/ and emb/CAA48394.1/)". (See page 64, lines 26-28). However, the specification does not teach what the sequence homology is between the translation products of this gene and the "glutathione peroxidase-related proteins" and specifically, there is no sequence homology data for Genbank Accession No CAA48394.1. It is noted that Table 2 (page 108) teaches a 67%

"Score/Percent Identity" of Genbank Accession No. CAB43534 from nucleotides 24 to 191 compared to SEQ ID NO: 22 (which encodes SEQ ID NO: 41). SEQ ID NO: 22 is 629 base pairs long, and therefore, the percent homology only represents the homology of a portion of SEQ ID NO: 22. It is also noted neither the specification, nor the prior art teach a well-established utility of Genbank Accession No. CAB43534. More specifically, Akasaka et al. (Nuc. Acid Res. (1990) 18(15): 4619) does not teach the specific activity of Genbank Accession No. CAB43534 or what Genbank Accession No. CAB43534 can be specifically used for (see also page 1 of the NCBI Sequence Viewer). At best, Akasaka et al. and the specification invite the skilled artisan to perform further experimentation to determine a real world context of use for Genbank Accession No. CAB43534 and SEQ ID NO: 41, and therefore, the claimed invention lacks a substantial utility (see MPEP 2107).

Next, the specification states, "this gene is expressed in colon or colon cancer tissue as determined by expression analysis described in Example 3." (See page 65, lines 27-28). Thus, the specification teaches that expression occurs in both normal colon and colon cancer tissue, and therefore, the expression of this gene is not specific for colon cancer, since this gene is expressed in normal colon tissue. Example 3 does not provide any further guidance. Specifically, Example 3 (on page 332), states, "Each of the genes described in Table 1 was determined to be selectively expressed in colon related tissues, including, but not limited to, colon cancer tissue by this method". First, it is not clear as to what is meant by or encompassed by "selectively expressed". Next, it is not clear as to what is encompassed by "colon related tissues". Finally, this gene is "selectively expressed" in tissues "including, *but not limited to*, colon cancer tissue", which means this gene is expressed in other colon related tissues, e.g.,

normal colon tissue, or some other colon related tissue. Accordingly, the specification does not teach or demonstrate the expression of this gene is specific for colon cancer, and at best, invites the skilled artisan to perform further experimentation to determine a real world context of use, and therefore, the claimed invention lacks a substantial utility (see MPEP 2107).

Next, the specification states, "this gene is expressed to a lesser extent in testis and other gastrointestinal tissues." (See page 65, lines 28-29) However, the specification does not teach or demonstrate any evidence of differential expression (e.g., between normal or cancerous testes tissue (or other gastrointestinal tissues)) or any other data that specifically correlates the expression of this gene and any disease or condition. Furthermore, the assertion that the gene is expressed "to a lesser extent" is also vague, since it is not clear as to what "a lesser extent" actually means, let alone whether expression "to a lesser extent" is significant for screening/assayable purposes.

The specification also states, "polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s)." (See page 66, lines 2-4) This asserted utility is not considered to be specific because no specific target is disclosed, and is not substantial because a skilled artisan would have to conduct further experimentation to find a specific target (see above and MPEP 2107.01).

The specification states further,

> For a number of disorders of the above tissues or cells, particularly of the gastrointestinal system, and/or reproductive systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., colon, gastrointestinal, reproductive, cancerous and wounded tissues) or bodily fluids (e.g., lymph, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

(page 66, lines 4-11). However, the specification does not teach whether the increased or decreased expression of this gene is detected in a specific disorder relative to the standard expression level in healthy tissue or bodily fluid from an individual not having the disorder. In fact, as discussed above, the specification asserts that there is expression in both normal colon and cancerous colon tissue. Thus, this passage does not define a substantial utility, as the skilled artisan would have to experiment to find a correlation between the claimed gene and a disease or disorder. See MPEP 2107.01. Furthermore, the general statement of using gene expression data for the comparison of diseased samples versus normal samples (e.g., reproductive, cancerous and wounded tissues) is applicable to any gene, and therefore, this utility is not considered to be specific.

On page 66, lines 16-22, the specification states,

> The tissue distribution in colon and colon cancer and homology with glutathione peroxidase proteins indicates that polynucleotides and polypeptides corresponding to this gene would be useful for diagnosis, treatment, prevention and/or detection of tumors, especially of the intestine, such as, carcinoid tumors, lymphomas, non-neoplastic polyps, adenomas, familial syndromes, colorectal carcinogenesis, colorectal carcinoma, cancer of the colon, cancer of the rectum and carcinoid tumors, as well as cancers in other tissues where expression has been indicated.

This assertion also lacks specific and substantial utility for several reasons. First, no homology data is present in the specification (except for GenBank Accession No. CAB43534, which has no specific activity or utility, see above), the specification only teaches that the translation products of this gene share "some" biological activity with other glutathione peroxidase proteins (of which no activity is taught), and no specific tumors of the intestine are correlated with the expression of the gene encoding SEQ ID NO: 41. Second, the specification does not provide any comparative expression data of normal or diseased samples of the claimed

gene. Finally, the skilled artisan would have to carry out further experimentation to correlate expression of the claimed gene and disease.

The specification also asserts "the expression in colon tissue may indicate the gene or its products can be used to treat, detect, prevent and/or diagnose" a laundry list of possible disorders. However, this assertion of treating disorders is not substantial because the skilled artisan would have to carry out further experimentation to correlate the expression of Gene 12, and a particular disease or disorder, and determine whether the translation products of this gene can be used in treatment of a particular disease or disorder.

Next, the specification states, "the protein may be used to show activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate interactions, in addition to its use as a nutritional supplement". (See page 67, lines 5-8) These utilities are not specific or substantial for several reasons. First, the specification does not teach any specific activity, antibodies, tissue markers, cognate ligands or receptors, agents that modulate interactions, or nutritional supplements. Furthermore, MPEP 2107.01 states, "a 'specific utility' is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention". Accordingly, these asserted utilities are not considered to be specific utilities, because these utilities are general utilities that would be applicable to a broad class of the invention (e.g., polypeptides). Finally, these utilities lack a substantial utility because the skilled artisan would have to carry out further experimentation to determine a real world context of use.

Finally, the specification states the, "protein...may show utility as tumor markers and/or immunotherapy targets for the above listed tissues." (page 67, lines 8-9). Again, as stated

above, this assertion lacks, at least, a substantial utility, as the specification does not specifically or reasonably correlate Gene 12, and any disease or condition. Therefore, the skilled artisan would have to carry out further experimentation to determine what tumor or immunotherapy target the translation products of Gene 12 can be used for.

Based on the foregoing analysis, the claimed invention is not supported by either a specific or substantial utility, or alternatively, a well-established utility, as the specification does not teach a specific or reasonable correlation between the gene (or its translation product) and any specific biological activity or use in disease/disorder detection or treatment.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 25, 28-33 and 36-40 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

7. Claims 25, 28-33 and 36-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

In the event the 101 and 112, 1st paragraph rejections (above) are withdrawn, the claimed invention fails to comply with the enablement requirement for the following reasons.

Nature and Breadth of the Invention

The claims are drawn to proteins of SEQ ID NO: 41 and compositions comprising proteins of SEQ ID NO: 41. The nature of this invention is a protein of a particular sequence with no associated activity. This is an invention in a subject area, which is well recognized as unpredictable.

Amount of Guidance in the Specification

The specification discloses the entire sequence of SEQ ID NO: 41, but identifies no particular activity or particular use for the sequence. Specifically, the specification teaches it can be used as a marker (i.e., diagnostic) for colon cancer, however, the specification teaches that the gene encoding this protein is expressed in both normal colon tissue and colon cancer tissue. The specification does not teach whether a particular level of expression is seen in normal versus colon cancer tissue, and therefore, the skilled artisan does not know how to determine whether a particular expression pattern is correlated with the diseased state. Accordingly, the specification does not provide the requisite guidance to enable a skilled artisan how to use SEQ ID NO: 41.

Working Examples

There are no detailed working examples in which SEQ ID NO: 41 is used in any assay for detection or diagnosis of any disease or any other related utility. Example 3, only concludes by stating, "Each of the genes described in Table 1 was determined to be selectively expressed in colon related tissues, including, but not limited to, colon cancer tissue by this method". Here, there is no guidance as to what is meant by or encompassed by "selectively expressed". Next, it is not clear as to what is encompassed by "colon related tissues". Finally, this gene is "selectively expressed" in tissues "including, *but not limited to*, colon cancer tissue", which means this gene is expressed in other colon related tissues, e.g., normal colon tissue, or some

other colon related tissue that is not specified in the specification. Accordingly, the specification does not working examples sufficient to enable the skilled artisan to use the claimed invention.

Amount of Guidance in Prior Art and the Relative Skill in the Art

The prior art provides no guidance with regard to the particular function of SEQ ID NO: 41. It is noted that although Applicants' teach that GenBank Accession No. CAB43534 has a 67% percent homology to a portion of the gene encoding SEQ ID NO: 41, the prior art does not teach what the activity of GenBank Accession No. CAB43534 is or what it can be used for.

Based on the lack of information in the specification and in the art regarding SEQ ID NO: 41, the relative skill in the art regarding the use of this protein is high.

Predictability of the Art

The art in biotechnology, as relates to the association of diseases with particular genes, is highly unpredictable. Given the limited expression data provided in the specification (e.g., expression in both normal colon tissue and colon cancer tissue) and the lack of a determined activity of the claimed protein, it is extremely unpredictable as to how to use SEQ ID NO: 41 in the absence of any clear guidance by the art or specification.

Quantity of Experimentation

An immense amount of experimentation would be required in order to define whether the protein is associated with any particular disease state. In order to acquire statistically significant evidence of an association with a disease or other utility, dozens of patients in each of the many hundreds of different possible disease states would need to be subjected to collection of samples for analysis of their DNA, followed by analysis and the inventive efforts of determining if any association exists. This is a very large quantity of experimentation.

Determination

In view of the unpredictable nature of the invention, the absence of any guidance in the specification, the absence of any detailed working examples in the specification, the lack of

teachings in the prior art, the extreme unpredictability of the invention, and the large amount of experimentation necessary balanced against the high level of skill in the art and the relatively narrow breadth of the claims, it is concluded that undue experimentation would be required to use this invention as claimed.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 25, 28-33 and 36-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Rosen et al. (US20020055627).

Rosen teaches SEQ ID NO: 1157, which is 100% identical to instant SEQ ID NO: 41 (see sequence search result #1). Rosen also teaches compositions comprising the claimed protein, methods of expressing the claimed protein, the protein comprising a heterologous polypeptide sequence, the protein is glycosylated, and the protein is fused to polyethylene glycol (see paragraphs 83, 115, 117, 128, 129, 132, 133, 138-147, and 151, for example)

10. Claims 25, 28-33 and 36-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Rosen et al. (US20030040617).

Rosen teaches SEQ ID NO: 1157, which is 100% identical to instant SEQ ID NO: 41 (see sequence search result #2). Rosen also teaches compositions comprising the claimed protein,

methods of expressing the claimed protein, the protein comprising a heterologous polypeptide sequence, the protein is glycosylated, and the protein is fused to polyethylene glycol (see paragraphs 85, 117, 119, 130, 131, 134, 135, 140-149, and 152-153, for example).

Conclusion

11. No claims are allowable.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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April 12, 2004

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